"Studies on Synthesis, Characterization and Biological investigation of Novel α,β Unsaturated Ketones and its derivatives"

A synopsis submitted to

Swami Ramanand Teerth Marathwada University, Nanded

(M.S.) India

For the degree of

DOCTOR OF PHILOSOPHY (Ph.D)

IN

CHEMISTRY

Under the faculty of sciences

By

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Ph.D. Synopsis

Subject : Chemistry

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Introduction of Proposed Research:

Chalcones – one of the major classes of natural products with widespread distribution in fruits, vegetables, spices, tea and soy based foodstuff, have been recently subjects of great interest for their interesting pharmacological activities[1]. Chalcones are belonged to the flavonoids family. A vast number of naturally occurring chalcones are polyhydroxylated in the aryl rings. The radical quenching properties of the phenolic groups present in many chalcones have raised interest in using the compounds or chalcone rich plant extracts as drugs or food preservatives[2]. Chalcones have been reported to possess many useful properties, including anti-inflammatory, antimicrobial, antifungal, antioxidant, cytotoxic, antitumor and anticancer activities. A number of chalcone derivatives, have also been found to inhibit several important enzymes in cellular systems, including xanthine oxidase[3], aldose reductase, epoxide hydrolase[4], protein tyrosine kinase[5] and quinone reductase[6]. Chalcones having an α, β unsaturated carbonyl group are one of the important biocides and versatile synthons for various chemical transformations. Most of the chalcones are highly biologically active with a number of pharmacological and medicinal applications[7]. Chalcones have been used as anti AIDS agents[8], cytotoxic agents with antimalarials, antiangiogenic activity[9], antiinfective and anti-inflammatory[10] and anti-tumor agents[11] . Some chalcones were found to increase the level of the tumor suppressor protein p53 in various cancer cell lines by disrupting its complexes with the oncoprotein MDM2[12] . Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine, pyrazolines[13], 1,4-diketones[14] and flavones[15]. Some heterocyclic systems based on chalcone precursors are benzothiazepines, benzodiazepines, benzoxazepines, pyrimidines, pyrazoles, and oxazoles[16] . Various substituted chalcones possess antioxidant[17], radicalscavenging[18], anticancer[19], antileishmanial[20], antimitotic[21], antitumor[22] and antibacterial[23] properties, as well as P-glycoprotein mediated multidrug resistance[24]

Literature Review of the Proposed Topic:

Development of novel synthetic routes to facilitate the preparation of desired molecule is an intense area of research. In this regard, efforts have been made constantly to introduce new methodologies which are efficient and more compatible with the environment. One of the most desirable approaches to address this challenge constitutes a search of surrogates for traditionally employed organic solvents which suffers from various health and environmental concerns.

The use of this synthesis of Chalcones compounds by using ionic liquids condition proved to be efficient, safe and environmentally benign technique, with shorter reaction time, high yields. Furthermore, it can also avoid the use of hazardous and expensive solvents and can be environmentally benign to make manipulations much easier.

Gaps in Existing Research:-

International Status:

It is of great interest and challenges for the researchers all over to design and develop new liquid liquid biphasic catalysis either a very efficient manner methodologies for the synthesis of bio-active compounds.

National status:

In view of the wide range of biological activities associated with the Chalcone compounds based on eco-friendly safer modem methods of reaction activation. Ionic catalysis technique for the Country like India as a great alternative to meet the demands of synthetic drugs.

Statement of Proposed Problem:-

The Chalcone compounds have great importance due to biological activities associated with them. The Chalcone compounds have wide application in physiological activities and industrial significance. There derivatives are useful in various fields like drugs, dyes, polymers, textile etc. In medicinal chemistry bioisosteric relation constitute one of the more familiar tools.

Scope of Research Work:

This research will provide a great alternative in future for the researchers and pharmacological industries to develop new procedures which are ecofriendly benign. Phase transfer catalyst is one the important and adaptable catalyst to achieve the goal of high yields, increased reaction rates, milder reaction conditions, cost efficient, readily available reagents, use

of simple equipments and easy workup procedures for the synthesis of new bio-active Chalcone compounds.

Relevance of the Research Work:

In recent times, the progress in the field liquid -liquid biphasic reaction is gaining significance because of their high efficiency,low time, operational simplicity and environmentally benign processes. Phase transfer Catalyst reactions based on grinding of two biphasic reaction mass together mostly involve the formation of a liquid phase prior to reaction.

Significance of the study:

This research will provide a great alternative in future for the researchers and pharmacological industries to develop new procedures which are eco-friendly benign. Phase transfer catalyst is one the important and adaptable catalyst to achieve the goal of high yields, increased reaction rates, milder reaction conditions, cost efficient, readily available reagents, use of simple equipments and easy workup procedures for the synthesis of new bio active Chalcone compounds.

Objectives of the Research:

We are interested in seeking new processes involving by using Phase transfer catalyst reactions, accompanied with many advantages. Organic synthesis in the presence of biophasic solvent is a powerful tool for the generation of structurally diverse molecules, due to their special selectivity, the ease of set-up and work-up, arousing great interest[25].Moreover, Phase transfer catalyst reactions sometimes are faster, taking just a contact with each other. This aspect, coupled with the lower overall costs of running a reaction with biophasic solvent and could become a decisive factor in industry . The drive for the development of media reactions in chemistry is economic, ease of purification (not required to maximum time), high reaction rate (due to high concentration of reactants) and environmentally friendly . Phase transfer catalyst reactions obviously reduce pollution, and bring down handling costs due to simplification of experimental procedure, work up technique and saving in labor. These would be especially important during industrial production[26].

Although most of these processes offer distinct advantages, they suffer from certain drawbacks such as longer reaction times, unsatisfactory yields, high costs, harsh reaction conditions and the use of a large quantity of volatile organic solvents[27]. Thus, the possibility of performing multi-component reactions under using green solvent like water PEG-400 and polymeric solvents could enhance their efficiency from an economic as well as a green point of view[28,29].

- Synthesis of new bioactive Chalcone compounds.

- Milder reaction conditions.
- Simple equipments required.
- Easily available cost efficient chemicals.

Hypothesis:

The steady growth in interest in chalcone compounds is basically connected with their raised biological activity and also with the fact that they enable the development of novel materials of unique properties. One very interesting and promising class of chalcone moiety due to both their use in medicinal chemistry as synthetic building block, and plays important role in biochemical process[30].

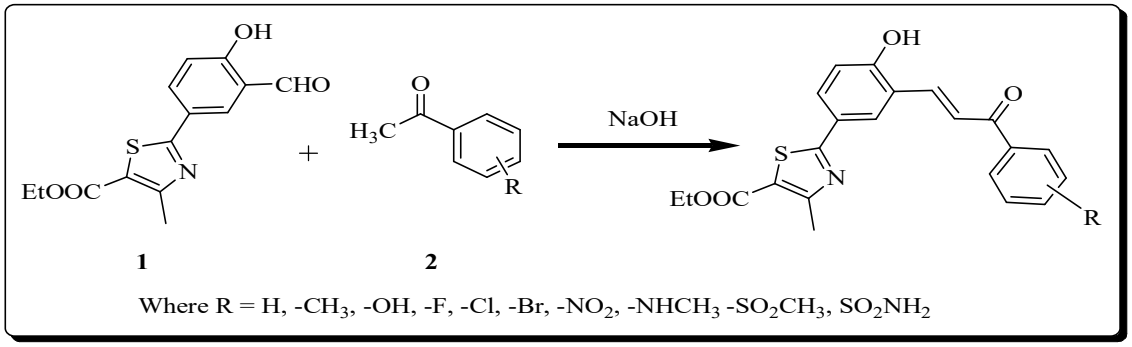
The chalcone compounds have physiological and industrial significance and thus have received significant attention for their preparation over decades. Most of modem drugs must contain the chalcone constituent and also have fewer side effects[31]. In recent years, chalcone compounds are an important class of organic compounds that find use as dyes, fluorescent material for visualization of biomolecules and in laser technologies due to their useful spectroscopic properties.The chalcone compounds have also received significant attention due to their useful biological and pharmacological properties, such as their such as treatment of viral disorders, cardiovascular diseases, parasitic infections, pain, gastritis, and stomach cancer, as well as like food additives and cosmetic formulation ingredients.The synthesized compounds will be characterized by analytical data as NMR, IR & MASS Study[32].

Research Methodology:-

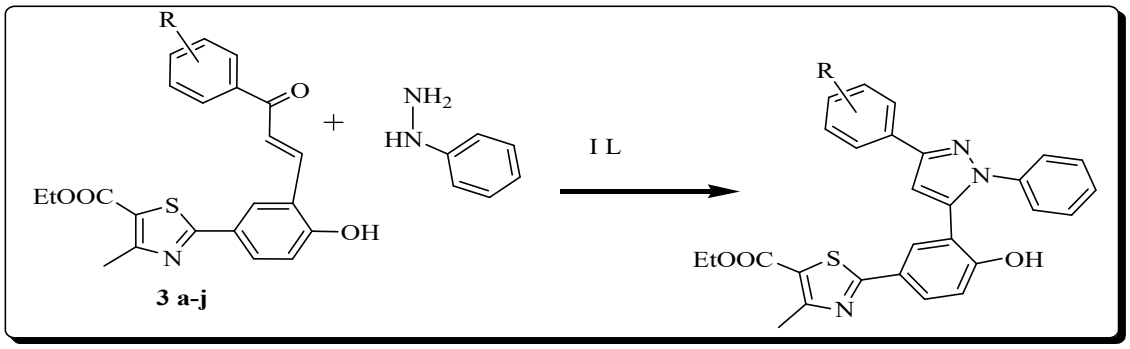
Development of green and Sustainable Phase transfer catalyst and study of their physical and chemical properties like hydrophilicity, hydrophobicity etc. Study of the effect of phase transfer catalyst on reaction, yield and byproducts obtain during use. Also study the application for more and more Chalcone compound synthesis.

Synthesis of novel Chalcones and its derivatives by using ionic liquids.

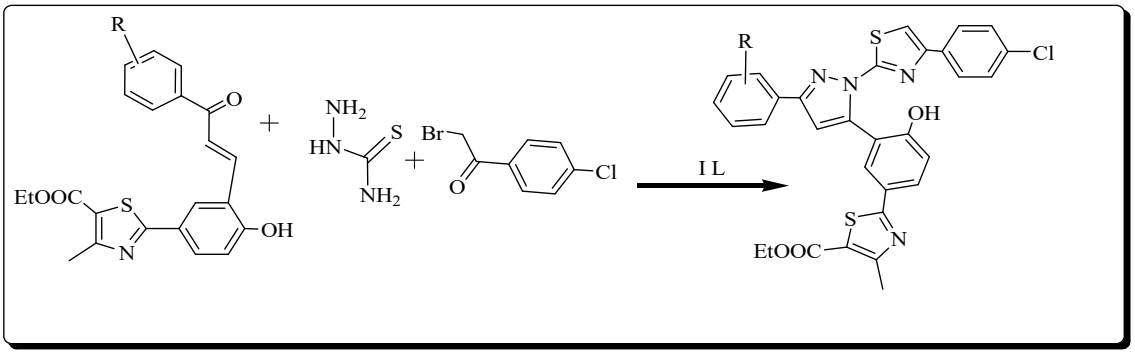
Scheme 1. Synthesis of Chalcones



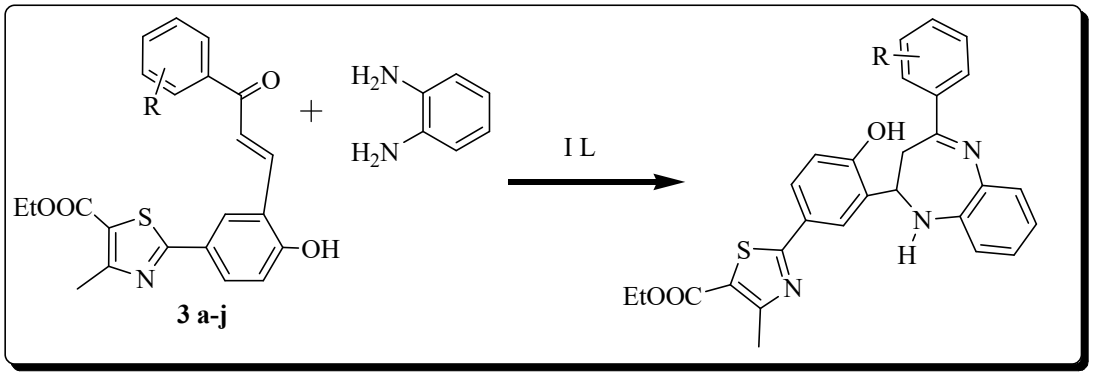
Scheme 2. Synthesis Pyrazolines



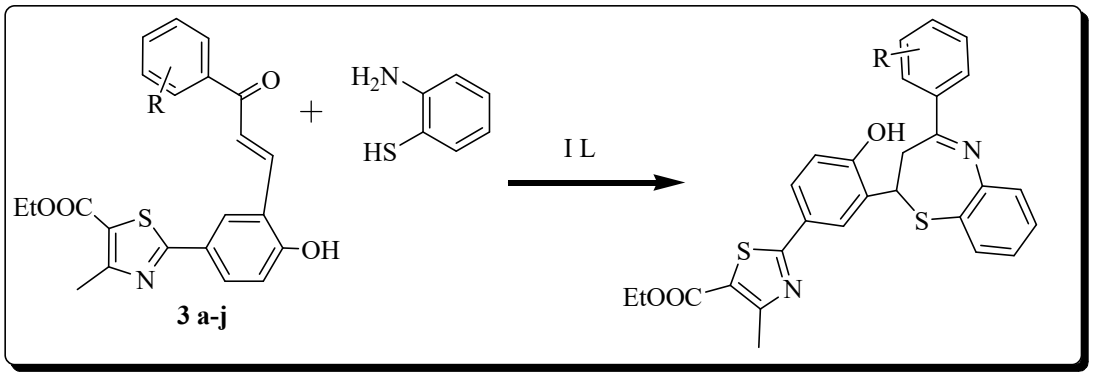
Scheme 3. Synthesis of thiazolyl Pyrazolines



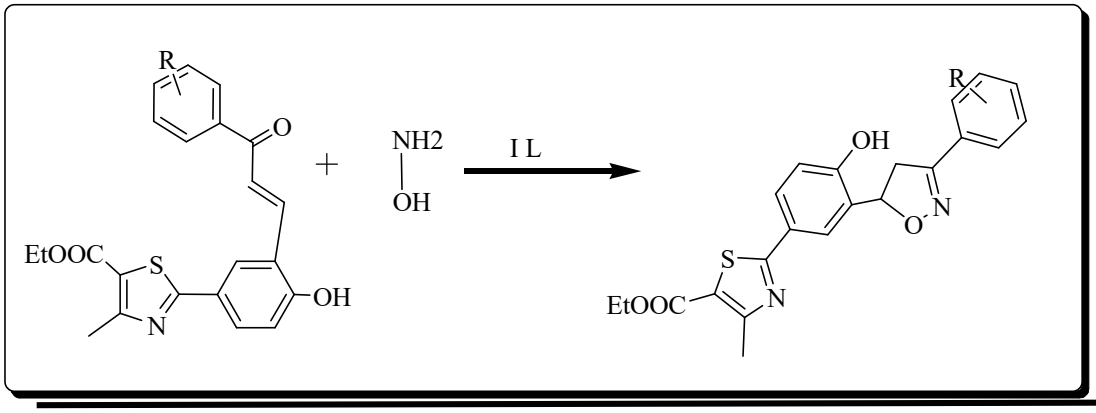
Scheme 4. Synthesis of benzodiazepines



Scheme 5. Synthesis of benzodiazepines



Scheme 6. Synthesis of benzodiazepines



Expected Outcome:-

We find the new roots to synthesis of these biologically active compounds with efficient yield and with normal reaction condition. The reactions are carried out from the simple and very common reactants which decrease the cost of the product. This includes Milder reaction conditions, Simple equipments required, Easily available cost efficient chemicals.

Plan of work:

I Year:

Literature Survey, final idea of the work, preliminary synthesis of some compounds

II Year:

Synthesis of Chalcone compounds by advance methods, using biphasic reaction media , water mediated reaction, dry media reactions and reaction using ecofriendly phase transfer catalyst catalysts, like enzymes nano materials etc.

III Year:

Purification of the compounds, analytical study of the compounds (IR, NMR, Mass), Publishing of the work and Thesis writing.

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